



#5P3
12/15/01 1631

Attorney Docket No. 20488/25-CIP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

RECEIVED
DEC 13 2001
TECH CENTER 1600/2900

APPLICANT: Pospisilik, et al.

U.S.S.N.: 09/932,546

Art Unit: 1631

FILED: 08/17/2001

Examiner: Unassigned

FOR: *USE OF DIPEPTIDYL PEPTIDASE IV EFFECTORS FOR LOWERING
BLOOD PRESSURE IN MAMMALS*

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as regular first class mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231 on November 19, 2001.

By:

Renee M. Mason

Renee M. Mason

INFORMATION DISCLOSURE STATEMENT

Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Pursuant to Applicant(s) duty of disclosure, the information listed in the attached form PTO-1449 is brought to the attention of the Examiner. Copies of the listed items are enclosed.

The citation of the listed items is not a representation that they constitute a complete or exhaustive listing of the relevant art or that the references are prior art. The items listed are submitted in good faith, but are not intended to substitute for the Examiner's search. It is hoped, however, that in addition to apprising the Examiner of these particular items, they will assist in identifying fields of search and in making as full and complete a search as possible.

The filing of this information disclosure statement is not an admission that the information cited herein is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

In accordance with the requirement under 37 C.F.R. 1.98 (3)(i), the following are concise explanations of the relevance, as presently understood, with regard to those items submitted herewith that are not in the English language:

I. LIST OF PATENTS, PUBLICATIONS OR OTHER INFORMATION

The patents, publications or other information submitted for consideration by the Office are listed on PTO-1449, attached hereto.

II. COPIES

- a. ☒ Submitted herewith is a legible copy of (i) each U.S and foreign patent; (ii) each publication or that portion which caused it to be listed; and (iii) all other information or that portion which caused it to be listed

III. CONCISE EXPLANATION OF THE RELEVANCE

(check at least one box)

- a. ☐ Except as may be indicated below in (b), all of the patents, publications or other information are in the English language or were cited in an English language Search Report, a copy of which is attached hereto (concise explanation not required).

- b. ☒ A concise explanation of the relevance of all patents, publications or other information listed that is not in the English language is as follows:

FRENCH LANGUAGE FR 2 696 740 apparently relates to Dimethylbiguanide drug derivatives and their medical applications.

FRENCH LANGUAGE FR 2 085 655 apparently relates to biguanide substitutes possessing a hypoglycemic property.

GERMAN LANGUAGE DT 25 42598 A1 apparently relates to biguanide salts as well as a method for preparing such salts. In addition to this the invention apparently covers pharmaceutical compounds which contain such salts.

GERMAN LANGUAGE DE 196 16 486 apparently relates to the use of a method for reducing in the blood of a mammal, by administration of effectors, the enzyme activity of dipeptidyl peptidase (DP IV) or enzyme activity similar to DP IV which causes the blood sugar level to drop below the glucose concentration, characteristic of hyperglycemia, in the serum of the treated organism; preventing or alleviating metabolic anomalies such as glucosuria, hyperlipidemia, possible serious metabolic acidosis, diabetes mellitus which result from higher concentrations of glucose in the blood.

GERMAN LANGUAGE WO97/40832 apparently relates to the use of a method for reducing in the blood of a mammal by administration of effectors the enzyme activity of dipeptidyl peptidase (DP IV) or enzyme activity similar to DP IV, the endogenous (or additionally exogenously administered) insulintropic peptide gastric inhibitory polypeptide 1-42

and glucagon-like peptide amide-1 7-36 are decomposed in a causal sequence to a reduced extent by DP IV enzymes or those similar to DP IV.

JAPANESE PATENT JP 4334357A2: ACYL DERIVATIVE HAVING ENZYME-INHIBITING ACTION, apparently relates to a compound having a prolyl endopeptidase activity-inhibiting action and useful as an antidement agent, especially an anti-amnestic agent.

- c. ☐ The following additional information is provided for the Examiner's consideration:

FEES

IV. THIS IDS IS BEING FILED UNDER 37 C.F.R. § 1.97(b)
(check one box)

- a. ☒ within three months of the filing date of a national application (37 C.F.R. § 1.97(b) (1)). No fee or certification is required.
- b. ☐ within three months of the date of entry of the national stage as set forth in §1.491 in an international application (37 C.F.R. § 1.97(b) (2)). No fee or certification is required.
- c. ☐ before the mailing date of a first Action on the merits (37 C.F.R. § 1.97(b) (3)). No fee or certification is required. In the event that a first Office Action on the merits has been issued, please consider this IDS under 37 C.F.R. § 1.97(c) and see the certification under 37 C.F.R. § 1.97(e) below, or, if no certification has been made, charge our deposit account a fee in the amount of \$180.00 as required by 37 C.F.R. § 1.17(p).

V. THIS IDS IS BEING FILED UNDER 37 C.F.R. § 1.97(c):
(check one box)

before the mailing date of a Final Office Action under 37 C.F.R. § 1.113 (See 37 C.F.R. § 1.97(c) (1)) or before the mailing date of a Notice of Allowance under 37 C.F.R. § 1.311 (See 37 C.F.R. § 1.97(c) (2)).

- a. ☐ No certification; therefore, a fee in the amount of \$180.00 is required by 37 C.F.R. § 1.17(p).
- or
- b. ☐ See the certification below. No fee is required.

VI. CERTIFICATION UNDER 37 C.F.R. § 1.97(e) (check only one box)

The undersigned hereby certifies that

- a. ☐ each item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application not more than three months prior to the filing of this IDS; or
 - b. ☐ no item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application or, to the best of my knowledge after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this statement.
 - c. ☐ Some of the items of information were cited in a communication from a foreign Patent Office as indicated in the Form 1449 by those references having an asterisk(). As to this information, the undersigned certifies that each item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application not more than three months prior to the filing of this IDS. As to the remaining information, the undersigned hereby certifies that no item of this remaining information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application or, to the best of my knowledge after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this statement.
- ☐ A check in the amount of \$180.00 is enclosed for the above-indicated fee. A duplicate copy of this paper is attached.
- ☒ No fee is required.
-

IDS USSN: 09/932,546

Page 6

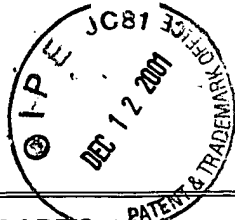
If the Examiner has any questions concerning this IDS, he/she is requested to contact the undersigned. If it is determined that this IDS has been filed under the wrong rule, the PTO is requested to consider this IDS under the proper rule (with a petition, if necessary) and charge the appropriate any additional fees to Deposit Account No. 50-0369.

Respectfully submitted,



Date: November 19, 2001

John C. Serio, Reg. No. 39,023
Brown Rudnick Freed & Gesmer
Customer No. 21710
One Financial Center
Boston, MA 02111
Tel: (617) 856-8238
Fax: (617) 856-8201



RECEIVED
TEC CENTER 1600/2900
DEC 13 2001

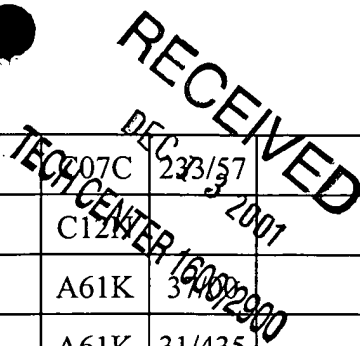
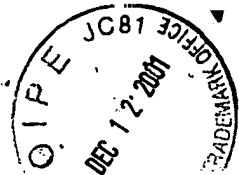
FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY DOCKET NO. 20488/25-CIP	SERIAL NO. 09/932,546
	APPLICANT(S): Pospisilik, et al.	
	FILING DATE: 08/17/2001	ART UNIT 1631

UNITED STATES PATENT DOCUMENTS

EXAM. INITIAL		DOCUMENT NUMBER	DATE	NAME	CLAS S	SUB CLAS S	FIL. DATE IF APPR
	AA	2,961,377	11-1960	Shapiro et al.	167	65	
	AB	3,960,949	6-1976	Ahrens et al.	260	564 B	
	AC	5,433,955	7-1995	Bredehorst et al.	424	94.3	
	AD	5,614,379	3-1997	MacKellar	435	68.1	
	AE	5,624,894	4-1997	Bodor	514	2	
	AF	4,935,493	6-1990	Bachovchin et al.	530	331	
	AG	5,512,549	4-1996	Chen et al.	514	12	
	AH	6,006,753	12-1999	Efendic	128	898	8/21/97

FOREIGN PATENT DOCUMENTS

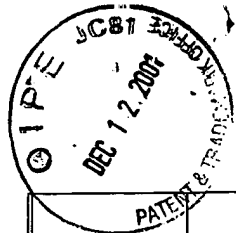
		DOCUMENT NUMBER	DATE	COUNTRY	CLAS S	SUB CLAS S	TRAN YES/N O
	BA	WO 00/53171 ✓	9-14-00	WO	A61K	31/155	
	BB	DT 25 42598 A1 ✓	10-11-74	Germany	C07C	129/16	
	BC	FR 2696740 ✓	10-13-92	France	C07D	207/40 4	
	BD	FR 2085665 ✓	3-3-71	France	A61K	27/00	
	BE	WO 97/40832 ✓	11/6/97	WO	A61K	31/425	
	BF	WO 95/15309 ✓	6/8/95	WO	C07D	207/16	



BG	4334357	✓	11/20/92	JP	C07C	233/57	
BH	WO 93/08259	✓	4/29/93	WO	C12K	31/435	
BI	WO 95/11689	✓	5/4/95	WO	A61K	31/435	
BJ	WO 97/45117	✓	12/4/97	WO	A61K	31/435	
BK	DE 19/616486	✓	10/30/97	DE	A61K	39/395	
BL	WO 95/29691	✓	11/09/95	WO	A61K	031/67 5	
BM	WO 98/22494	✓	5/28/98	WO	C07K	005/00	
BN	PCT 00/01849	✓	7/20/00	PCT	A61K	31/155	

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)

CA	Campbell, I.W. "New antidiabetic drugs, Sulphonylureas and metformin: efficacy and inadequacy". 3:33-51 (1990). SMITH-GORDON, NISHIMURA; "Sulphonylureas and Metformin: Efficacy and Inadequacy." 9/7/01, Page 36						✓
CB	Mercla Index, 11 th Edition, Page 934						✓
CC	Martindale the Extra, Pharmacopeia, Page 1619						✓
CD	CHEMICAL ABSTRACTS, vol. 115. No. 15, 14. October 1991 (1991-10-14) Columbus, Ohio, US; abstract no. 149947q, SCHOEN EKKEHARD ET AL: "Dipeptidyl peptidase IV in the immune system. Effects of specific enzyme inhibitors on activity of dipeptidyl peptidase IV and proliferation of human lymphocytes" Suite 37; XP002114197 Zusammenfassung & BIOL. CHEM. HOPPE-SEYLER, Bd. 372, Nr. 5, 1991, Seiten 305-311,						✓
CE	CHEMICAL ABSTRACTS, vol. 126, no. 2, 13. January 1997 (1997-01-13) Columbus, Ohio, US; abstract no. 16161j, STOECKEL A. ET AL: "Competitive inhibition of proline specific enzymes by amino acid thioxopyrrolidides and thiazolidides" Seite 241; XP002114198 Zusammenfassung & PEPT: CHEM., STRUCT.BIOL., PROC.AM.PEPT.SYMP., Nr. 14, 1995, Seiten 709-710,						✓
CF	CHEMICAL ABSTRACTS, vol. 118, no. 25, 21. Juni 1993 (1993-06-21) Columbus, Ohio, US; abstract no. 255342k, Hosed, et al, "Preparation of N-(heterocyclic Carbonyl) Amen Acids and Analogs as Prolyl Endopeptidase Inhibitors". Seite 933; XP002114199 Zusammenfassung & JP 04 334357 A (FUJEREBIO INC) 20. November 1992 (1992-11-20)						✓
CG	HEIHACHIRO ET AL: "Synthesis of prolyl endopeptidase inhibitors and evaluation of their structure-activity relationships : in vitro inhibition of prolyl endopeptidase from Caning Brain" CHEMICAL AND PHARMACEUTICAL BULLETIN., Bd. 41, Nr. 9,						✓



		1993, Seiten 1583-1588, XP002114196 PHARMACEUTICAL SOCIETY OF JAPAN. TOKYO., JP ISSN: 0009-2363 das ganze Dokument
	CH	J. Lin et al.: "Inhibition of depeptidyl peptidase IV by fluoroolefin-containing n-peptidyl-0-hydroxylamine peptidomimetics" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, Bd. 95, November 1998 (1998-11), Pages 14023-14024, XP002117450 WASHINGTON US Seite 14023, rechte Spalte, Absatz 1, linke Spalte, Absatz 1
	CI	KOROM, S., et al "Inhibition of CD26/dipeptidyl peptidase IV activity in vivo prolongs cardiac allograft survival in rat recipients, Transplantation 63", 1495 - 1500 No. 10 (1997)
	CJ	TANKA, S., et al., "Suppression of arthritis by the inhibitors of dipeptidyl peptidase IV". Int. J. Immunopharmacol". 19, 15 (1997), Vol 19 No. 1 Pages 15-24, 1997
	CK	MENTLEIN, R., DAHMS, P., GRANDT, D., KRUGER, R., "Proteolytic processing of neuropeptide Y and peptide YY by dipeptidyl peptidase IV". Regul. Pept. 49, 133 - 144(1993)
	CL	WETZL, W., WAGNER, T., VOGEL, D., DEMUTH, H.-U., BALSCHUN, D., "Effects of the CLIP fragment ACTH 20-24 on the duration of REM sleep episodes". Neuropeptides, 31, 41- 45 (1997)
	CM	AMASHEH, S., WENZEL, U., WEBER, W.M., CLAUSS, W., DANIEL, H., "Electrophysiological analysis of the function of the mammalian renal peptide transporter expressed in Xenopus Laevis oocytes". J. Physiol. 504, 169-174 (1997)
	CN	WAKSELMAN, M., NGUYEN, C., MAZALEYRAT, J.-P., CALLEBAUT, C., KRUST, B., HOVANESSIAN, A.G., "Inhibition of HIV-1 infection of CD 26+ but not CD26-cells. by a potent cyclopeptidic inhibitor of the DPP IV activity of CD 26. Abstract P 44 of the 24th European Peptide Symposium 1996."
	CO	DURINX, C.; NEELS, H.; VAN DER AUWERA, JC.; NAELAERS, K.; SCHARPE. S.; DE MEESER I.; "Reference Values for Plasma Dipeptidyl-Pepidase IV activity and their Association with Other Laboratory Parameters". Clin Chem Lab Med 2001, February; 39 (2) :155-9, 1 Page.
	CP	GOSSRAU, R.; "Cytochemistry of Membrane Proteases". Histochem J, 1985, July; 17 (7) :737-71, 1 Page..
	CQ	HAHN, T.; GRAF, R.; ONEY, T.; "Enzyme Histochemical Evidence for the Presence of Potential Blood Pressure Regulating Proteases in Cultured Villous Explants from Human First Trimester Placentae". Acta Histochem 1993, December, 1995 (2):185-92.
	CR	HEYMANN, E.; MENTLEIN, R.; "Has Dipeptidyl Peptidase IV an Effect on Blood Pressure and Coagulation". Klin Wochenschr, 1984, January, 2;62 (1) :2-10.
	CS	MAGYAR, C.E.; ZHANG, Y.; HOLSTEIN-RATHLOU, N.H.; MCDONOUGH, A.A.; "Proximal Tubule Na Transporter Responses are the same during Acute and Chronic

RECEIVED
DEC 12 2007
TECH CENTER 1500/2900

		Hypertension.” Am J Physiol Renal Physiol, 2000, August; 279 (2) :F358-69, 1 Page.
	CT	PAPIES, B.; FRILLE, J.; GUNTHER, K.H.; WAGENKNECHT, C.; Isoenzyme (Lactate “Dehydrogenase, Aspartate Aminotransferase) and Dipeptidyl Peptidase IV Activity Changes in Blood Plasma Likely Indicative of Organ Involvement due to Arterial Hypertension.” Cor Vasa, 1991; 33 (3) :218-26, 1 Page.
	CU	QURESJO. N.U.; DAYAO, E.K.; SHIRALI, S.; ZUKOWSKA-GROJEC, Z.; HAUSER, G. J., “Endogenous Neuropeptide Y Mediates Vasoconstriction during Endotoxic and Hemorrhagic Shock”. Regul Pept, 1998, September 25; 75-76:215-20, 1 Page.
	CV	Index Nominum, International Drug Directory 1992/1993, Medpharm Scientific Publishers, Pages 728-729.
	CW	The Merck Index, 9 th Edition, 1976, Page 773
Examiner:		Date:

#1066451 v\1 - seriojc□ - %vn01!.doc□ - 20488/25-CIP